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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/508,762	09/22/2004	Joseph Anthony Jakubowski	X-15632	9672

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EXAMINER	
AUDET, MAURY A	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 10/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/508,762	JAKUBOWSKI ET AL.	
	Examiner	Art Unit	
	Maury Audet	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response (no amendment) of 08/07/06, is acknowledged. Claims 1-15 are pending and examined on the merits (claim 1 being the only independent claim).

Specification

As noted in the previous action (though no addressing of this issue was found), the abstract of the disclosure does not commence on a separate sheet in accordance with 37 CFR 1.52(b)(4). A new abstract of the disclosure is required and must be presented on a separate sheet, apart from any other text. Although the file contains a copy of the abstract as presented in the International Application (PCTUS03/08457, WO 03/087139), it has not been submitted on a separate sheet in accordance with 37 CFR 1.52(b)(4).

Claim Rejections - 35 U.S.C. § 112 1st Enablement

The rejection of claims 1-15 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, is maintained for the reasons of record. Applicant's arguments have been considered but are not found persuasive. The substance of Applicant's arguments (minus boilerplate case law recitation on Enablement) spans a total of 4 sentences. Therein, Applicant appears to assert the following (very similar to the conclusory specification and presently claimed invention):

1. That even though no tests have been performed on the use of any GLP-1 compound to treat gastroparetic patients (e.g. the claimed invention), that Figures 1 and 2 on *glucose*

concentrations using GLP-1 in *non-gastroparetic patients* provide ample enablement for the present invention; and

2. That the Examiner has not provided any *evidence* why human clinical data showing that administration of GLP-1 compounds that results in normalizing gastric emptying would NOT be effective treatment for patients suffering from gastroparesis AND that this shifts the burden back to the Office.

This is found to be wholly unpersuasive. The Examiner has clearly shown the prior art of record does not teach GLP-1 as enabled for gastroparesis (see below for convenience), thus satisfying our burden. Applicant has provided no testing commensurate in scope with determining whether the present invention is enabled. Arguably blind conclusions thereto are not sufficient enablement. When enablement is in question, the general rule (absent *evidence* to the contrary, which the Office provided here based on contradictory teachings in the art) that the Office must 'assume' a specification is enabled (in line with *In re Marzocchi*) no longer applies. The Office does not have sufficient time or resources to conduct laboratory tests to determine whether Applicant's invention(s) works or not. The burden properly remains with Applicant to show *evidence* that this invention is enabled.

[The substance of the rejection is included below, once again, for continuity of the record and ease of accessibility to Applicant in responding hereto.]

The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant disclosure fails to meet the enablement requirement for a method of treating gastroparesis in a patient suffering therefrom comprising an effective amount of a GLP-1 compound, for the following reasons:

The nature of the invention: A method of treating gastroparesis in a patient suffering therefrom comprising an effective amount of a GLP-1 compound.

The state of the prior art and the predictability or lack thereof in the art:

> Gastroparesis is defined as "A condition where there is delayed stomach emptying (due abnormal gastric motility), often see as a complication of diabetes mellitus. Risk factors include diabetes, systemic sclerosis, previous vagotomy, previous gastrectomy, viceral neuropathy and the use of anticholinergic medications. Symptoms include bloating, nausea, vomiting and constipation. Treatment include dietary modification and the use of cholinergic medications and metachlopromide (http://cancerweb.ncl.ac.uk/cgi-bin/omd?query=gastroparesis, 09/27/1997).
>
> Schira et al. describe that GLP-1 is a gut hormone released postprandially and that synthetic GLP-1 is known to strongly inhibit gastric emptying in healthy subjects and in patients with diabetes mellitus; as well as antro-pylori-duodenal motility in humans. (Gut 2000, 46:622-31, abstract).

The amount of direction or guidance present and the presence or absence of working examples: Enablement must be provided by the specification unless it is well known in the art. *In re Buchner* 18 USPQ 2d 1331 (Fed. Cir. 1991). The specification cites a number of references that mirror the teachings of Schira et al. discussed above, but go on to describe that "[g]iven that GLP-1 has been shown to actually cause a delay in gastric emptying and inhibit smooth muscle contraction, it is surprising that the peptide can be used to treat gastroparesis which is a disorder thought to be caused by decreased contractility and delays in gastric emptying" (page 3, lines 19-22). A search of the specification did not indicate how or what variables lead Applicant to the latter "discovery". The only figures (1 and 2) are directed to the mean glucose concentrations

following once-daily administration of a GLP-1 analog in a patient with type 2 diabetes (page 4, lines 5-11). However, it is later described, that the studies of figures 1 and 2 "*suggest* that administration of GLP-1 compound to *type 2 diabetic patients without symptomatic gastroparesis* does not delay gastric emptying compared to placebo [and] GLP-1 compounds *may not delay gastric emptying* and instead normalize gastric emptying such that patients no longer experience one or more of the symptoms associated with gastroparesis" (page 5, lines 28-32 to page 6, lines 1-2).

In other words, the specification describes testing *non-gastroparetic* diabetic type 2 patients for glucose levels following GLP-1 administration. From this data, Applicant surmises that the test results *suggest* that gastric motility in *non-gastroparetic* patients is not affected by GLP-1 administration. Taking one more step, Applicant then concludes that GLP-1 compound may not delay gastric emptying, and thus *may* treat (e.g. normalize) gastric emptying in gastroparetic patients.

The breadth of the claims and the quantity of experimentation needed: The claims are drawn broadly to a method of treating gastroparesis in a patient suffering therefrom comprising an effective amount of a GLP-1 compound. Although Applicant may have added to the literature base by showing that GLP-1 may not inhibit gastric motility *in healthy, non-gastroparetic subjects*, there is no guidance in the present description single study on glucose concentrations after GLP-1 administration, that would enable one of ordinary skill in the art to administer a GLP-1 compound to somehow increase gastric motility and thus treat a subject who suffers from a disorder where gastric motility is known to be substantially reduced through an unknown genetic/environmentally-induced pathology. Based on the highly unpredictable and

complex nature of treating gastroparesis, and it's unknown origin/pathway (compounded by the fact that Applicant has not even tested the GLP-1 compounds claimed in a patient bearing symptoms of gastroparesis); it is concluded that absent sufficient teachings in the specification or art sufficient to overcome the teachings of unpredictability in the art as to enablement on whether a GLP-1 compound is even a targeting agent of the unknown etiological biochemical pathway of gastroparesis, it would require undue experimentation by one of skill in the art to be able to practice the invention commensurate in scope with the claims.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maury Audet whose telephone number is 571-272-0960. The examiner can normally be reached on M-Th. 7AM-5:30PM (10 Hrs.).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecelia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MA, 10/13/2006

CHRISTOPHER R. TATE
PRIMARY EXAMINER